REMARKS

Applicants respectfully request reconsideration of this application, and reconsideration of the Office Action dated May 20, 2003 (Paper No. 21). Upon entry of this Amendment, claims 1, 10, and 17-19 will remain pending in this application. The amendments to the claims are fully supported by the specification and original claims. No new matter is incorporated by this Amendment.

Applicants wish to thank Examiner Bernhardt for the courtesies extended to Applicants' representative during the interview of July 29, 2003. During the interview, the prior art as well as the Barkóczy declaration were discussed. However, an agreement as to the patentability of the claims was not reached.

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Claims 1, 9, 10, and 19 are rejected under 35 U.S.C. § 112, second paragraph as indefinite. Applicants respectfully traverse.

The Office Action asserted that the salt-forming step originally recited in the claims is no longer in the claims, yet the claims still recite that salts are made. In response, Applicants have amended independent claim 1 by reintroducing the salt forming step originally included in the claim. Hence, the amendment does not introduce new matter.

The Office Action also asserted that claim 9 is indefinite because it recites alternate routes no longer claimed in independent claim 1. Claim 9 has been cancelled by this amendment thereby rendering this part of the rejection moot.

Finally, the Office Action asserted the word "reactants" should be singular. In response, Applicants have amended claim 19 as suggested by the Examiner.

Applicants submit that the above remarks address this rejection. Hence, reconsideration and withdrawal of the rejection are respectfully requested.

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The rejection of claims 1, 9, 10, and 17-19 under 35 U.S.C. § 103(a) as purportedly obvious based on Zara (GB 2 262 526) is maintained. Applicants again respectfully traverse this rejection.

In maintaining the rejection, the Office Action asserted that while the declaration filed under 37 CFR § 1.132 showed superior results for the compound produced by the claimed process, the reaction conditions (solvent, temperature, amount of reactants) were not set forth. The Office Action asked whether a solvent was employed. The Examiner's comments on the interview summary also asserted that the reaction conditions for obtaining the instant compound were not clearly set forth.

As an initial matter, Applicants note that they have amended claim 1 to include certain reaction conditions. For example, claim 1, as amended, recites that the reaction is carried out in a dipolar aprotic solvent in the presence of an acid binding protein.

Applicants respectfully submit it is unforeseen that the compound of general formula II reacts with the compound of the general Formula VI in only an alkylation reaction, while the N-H group of the pyridazinone ring does not participate in the reaction under the condition applied in the claimed process. Contrary to the assertions made in the last Office Action, the Barkóczy declaration clearly shows that when reacting the compound of Formula II with the compound of formula VI under the Zara reaction conditions, an oily product was obtained which contained only 84.7% of the desired compound of Formula I and also 3.7% of a dimer contamination of the following formula:

(see bottom of page 2 of Sep. 19, 2003 letter)

The above dimer is formed in the alkylation reaction of the N-H group of the pyridazinone ring.

The compound produced by the Zara method cannot be compared to the presently claimed method. This is because of the fundamental and drastic difference that in Zara's method the nitrogen is protected by a methyl group. Thus, the nitrogen is chemically

excluded from reacting to form by-products. Since the formation of by-products is prevented by the methyl protected nitrogen, the method of Zara can be carried out in drastic conditions (e.g., Zara's reaction can be carried out in a melt at 120° C.)

In contrast, the starting material of the presently claimed method employs a reagent of the general Formula II which contains an unprotected nitrogen. Thus, the reaction is carried out under milder reaction conditions (i.e., in a dipolar aprotic solvent and in the presence of an acid binding agent as recited in independent claim 1).

The presence of large amounts of impurities is unallowable under the present stringent requirement of Pharmacopoeia. Thus, in the Barkóczy declaration, the reagents of the presently claimed method were reacted under the conditions described by Zara thereby showing that under the Zara conditions the present invention could not be carried out in a proper and pharmaceutically suitable manner. Hence, the Barkóczy declaration clearly shows that those of ordinary skill in the art would have been dissuaded from carrying out the presently claimed method according to the teachings of Zara. Zara simply fails to teach employing the claimed reagents in the claimed method under the claimed conditions. Moreover, in view of the Barkóczy declaration, there is nothing in the teachings of Zara which would provide the requisite motivations to those of ordinary skill in the art to modify the teachings of Zara as suggested in the Office Action. Those of ordinary skill in the art would simply have no expectation of success as shown by the Barkóczy declaration.

Applicants note the Examiner's confusion with respect to the indication in the Barkóczy declaration that the presently claimed method resulted in a yield of 99.78% of the desired compound, whereas example 4 indicates a 59% yield. Applicants point out that the numerical value of 99.78% does not represent the yield of the reaction but the purity of the sample. In other words, the purity of the sample is 99.78% according to the results of the HPLC-MS analysis.

The above remarks overcome this rejection. Hence, reconsideration and withdrawal of the rejection are respectfully requested.

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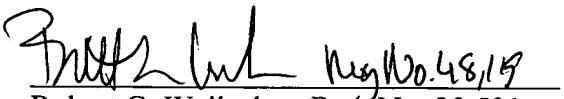
Applicants respectfully submit that this Amendment and the above remarks obviate the outstanding rejections in this case, thereby placing the application in condition for immediate allowance. Allowance of this application is earnestly solicited.

If any fees under 37 CFR §§1.16 or 1.17 are due in connection with this filing, please charge the fees to Deposit Account No. 02-4300; Order No. 032340.004.

If an extension of time under 37 CFR § 1.136 is necessary that is not accounted for in the papers filed herewith, such an extension is requested. The extension fee should be charged to Deposit Account No. 02-4300; Order No. 032340.004.

Respectfully submitted,

SMITH, GAMBRELL & RUSSELL, LLP

By:  Reg No. 48,19
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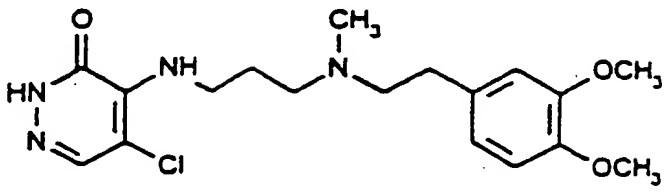
RGW/BLN

LISTING OF CLAIMS

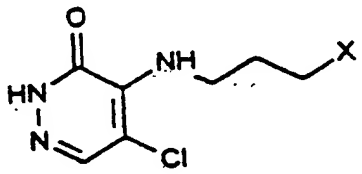
Claim 1 (currently amended): A process for the preparation of 5-chloro-4-{3-[n- [2- (3,4-dimethoxyphenyl) –ethyl] –N- methylaminol –propylamino} –3 (2H) – pyridazinone of the formula (I)



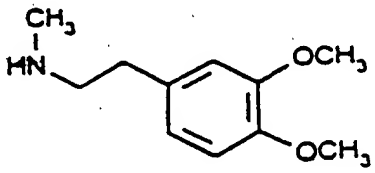
~~and pharmaceutically acceptable acid addition salts thereof~~,

which comprises

a1) reacting, in a dipolar aprotic solvent in the presence of an acid binding agent, a compound of the general formula (II),



wherein X stands for a leaving group, with N-methyl-homoveratryl amine of the formula (VI);



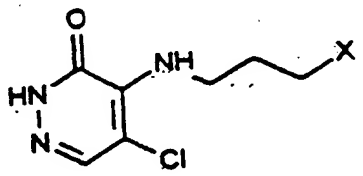
and, if desired, converting the thus obtained compound of formula (I) into an acid addition salt thereof.

Claims 2-9 (cancelled)

Claim 10 (currently amended): A process as claimed in claim ~~9~~ 1, ~~which comprises using~~ ~~as~~ said solvent is acetone, acetonitrile, or dimethylformamide and ~~as~~ said acid binding agent is an alkali carbonate, an alkali hydrogen carbonate or an amine.

Claims 11-16 (Cancelled)

Claim 17 (previously amended): A compound of the general formula (II),



wherein X stands for a leaving group.

Claim 18 (original): A compound of the general formula (II) according to claim 17, wherein X stands for bromine.

Claim 19 (currently amended): A process as claimed in claim 10, wherein the amine is triethylamine or an excess of the ~~reagents~~ reagent of formula (VI).